

<i>Inputs</i>	<i>Carbohydrate availability</i>	<i>AA/N<sub>2</sub> metabolism</i>	<i>Quorum Sense</i>	<i>AMPs</i>	<i>Metal</i>	<i>Regulators</i>
CovR/S	X	X	X		X	X
VicR/S				X		X
CiaHR		X	X			
Sil						X
TrxR/S				X		X
FasBCA(X)	X		X	X		
SptR/S					X	
Ihk/Irr		X		X	X	X
	Oxidative/Acid Stress	PMN	Non- immune cells	Blood	Saliva	Animal models

**Supplemental Table 1. Control of TCS regulators of virulence in *S. pyogenes*.** Inputs affecting regulator activity (colored fields) as well as environments/conditions in which expression of these regulators is observed (X) are shown. Colors correspond to categories across all tables (**Carbon utilization**, **AA/N<sub>2</sub> metabolism**, **Growth phase/Quorum sensing**, **Stress Response**, **Virulence**, **Biosynthesis**, **Regulation**).

<i>Downstream pathways affected</i>	<i>Carbon Utilization</i>	<i>AA/N<sub>2</sub> metabolism</i>	<i>Growth phase/ Quorum Sensing</i>	<i>Stress response</i>	<i>Virulence</i>	<i>Biosynthesis</i>	<i>Regulation</i>
CovR/S							
VicR/K							
CiaHR							
Sil							
TrxR/S							
FasBCA(X)							
SptR/S							
Ihk/Irr							

**Supplemental Table 2. Activity of TCS regulators of virulence in *S. pyogenes*.** The categories of downstream effectors influenced by TCS regulator activity in *S. pyogenes* (colored fields) are shown. Colors correspond to categories across all tables.

<i>Inputs</i>	<i>Carbohydrate</i>	<i>AA/N<sub>2</sub></i>	<i>Growth phase/ Quorum Sensing</i>	<i>AMPs</i>	<i>Metal</i>	<i>Regulators</i>
RALPs (RofA, RivR, RALP3, Nra)			X	X	X	X
CcpA					X	X
LacD.1						
Mga				X		X
RelA (Rsh <sub>str</sub> )						
CodY				X		
MtsR	X					X
Rgg/RopB	X					
PerR	X	X		X	X	X
Srv						X
Rgg2/3						
MalR			X		X	X
MsmR						
	Oxidative/Acid Stress	PMN	Non- immune cells	Blood	Saliva	Animal models

**Supplemental Table 3. Control of transcriptional regulators of virulence in *S. pyogenes*.** Inputs that affect regulator activity (colored fields) as well as environments/conditions in which expression of these regulators is observed (X) are shown. Colors correspond to categories across all tables.

<i>Downstream pathways affected</i>	<i>Carbon Utilization</i>	<i>AA/N<sub>2</sub> metabolism</i>	<i>Metal Homeostasis</i>	<i>Growth phase/ Quorum Sensing</i>	<i>Stress response</i>	<i>Virulence</i>	<i>Biosynthesis</i>	<i>Regulation</i>
<b>RALPs (RofA, RivR, RALP3, Nra)</b>								
<b>CcpA</b>								
<b>LacD.1</b>								
<b>Mga</b>								
<b>RelA (Rsh<sub>str</sub>)</b>								
<b>CodY</b>								
<b>MtsR</b>								
<b>Rgg/RopB</b>								
<b>PerR</b>								
<b>Srv</b>								
<b>Rgg2/3</b>								
<b>MsmR</b>								

**Supplemental Table 4. Activity of transcriptional regulators of virulence in *S. pyogenes*.** The categories of downstream effectors influenced by transcriptional regulator activity (colored fields) are shown. Colors correspond to categories across all tables.